PATENT COOPERATION TREATY EP04788979

PCT

– INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 28967/39670A	**FOR FURTHER ACTION**	See Form PCT/IPEA/416
International application No. PCT/US2004/031318	International filing date *(day/month/year)* 23.09.2004	Priority date *(day/month/year)* 23.09.2003

International Patent Classification (IPC) or national classification and IPC
A61K38/18

Applicant
LUDWIG INSTITUTE FOR CANCER RESEARCH

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 8 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☐ *sent to the applicant and to the International Bureau)* a total of sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in Item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:
   - ☒ Box No. I Basis of the opinion
   - ☐ Box No. II Priority
   - ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - ☐ Box No. IV Lack of unity of invention
   - ☒ Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - ☐ Box No. VI Certain documents cited
   - ☐ Box No. VII Certain defects in the international application
   - ☒ Box No. VIII Certain observations on the international application

Date of submission of the demand	Date of completion of this report
23.07.2005	10.10.2005
Name and mailing address of the International preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Didelon, F Telephone No. +49 89 2399-7332

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International application No. PCT/US2004/031318

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
   - ☐ international search (under Rules 12.3 and 23.1(b))
   - ☐ publication of the international application (under Rule 12.4)
   - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

Description, Pages	
1-136	as originally filed
Claims, Numbers	
1-80	as originally filed
Drawings, Sheets	
1/1	as originally filed

   ☒ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

* *If item 4 applies, some or all of these sheets may be marked "superseded."*

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Supplemental Box relating to Sequence Listing

Continuation of Box I, item 2:

1. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this report has been established on the basis of:

   a. type of material:

   ☒ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☒ in written format

   ☒ in computer readable form

   c. time of filing/furnishing:

   ☒ contained in the international application as filed

   ☒ filed together with the international application in computer readable form

   ☐ furnished subsequently to this Authority for the purposes of search and/or examination

   ☐ received by this Authority as an amendment on

2. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional observations, if necessary:

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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 13-24,26-57,59-63,70-73 (IA)

because:

☒ the said international application, or the said claims Nos. 13-24,26-57,59-63,70-73 relate to the following subject matter which does not require an international preliminary examination (specify):

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos.

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form ☐ has not been furnished

☐ does not comply with the standard

the computer readable form ☐ has not been furnished

☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

Form PCT/IPEA/409 (January 2004)

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Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	42,43,51,52
	No:	Claims	1-4,44-50,53-80
Inventive step (IS)	Yes:	Claims	-
	No:	Claims	1-80
Industrial applicability (IA)	Yes:	Claims	1-12,25,58,64-69,74-80
	No:	Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Form PCT/IPEA/409 (January 2004)

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (SEPARATE SHEET)

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Re Item III.

Claims 13-24,26-57,59-63,70-73 relate to methods of treatment of the human/animal body which is subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

Re Item V.

1. Reference is made to the following documents:

D1 : WO 01/76620 A (VLAAMS INTERUNIVERSITAIR INSTITUUT VOOR BIOTECNOLOGIE VZW; D. COLLEN R) 18 October 2001 (2001-10-18)

D2 : WO 03/024478 A (NEURONOVA AB; DELFANI, KIOUMARS; JANSON, ANN, MARIE; KUHN, GEORG, H; P) 27 March 2003 (2003-03-27)

D3: JOUKOV V et al.: "A recombinant mutant vascular growth factor-C that has lost VEGFR-2 binding, activation, and vascular permeability activities" JOURNAL OF BIOLOGICAL CHEMISTRY, AMERICAN SOCIETY OF BIOLOGICAL CHEMISTS, BALTIMORE, MD, US, vol. 273, no. 12, 20 March 1998 (1998-03-20), pages 6599-6602, XP002066366 ISSN: 0021-9258

Unless otherwise indicated, the relevant passages in the cited documents are the ones indicated in the Search Report.

2. Novelty:

2.1 The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claims 1-41, 44-50,53-80 is not new in the sense of Article 33(2) PCT.

Document D1 and D2 both disclose VEGF-C and -D which are presented, among others, as homologues of VEGF are envisaged to be useful in the treatment of neuronal or motoneuronal disorders. Although it does not exemplify the use of VEGF-C or -D for

treating neural disorders, D1 unambiguously considers that said factors are able to treat the neuronal disorders cited.
In addition, D2 also contemplates the combination of VEGFs with other neural growth factors, such as PDGFs.

D1 and D2 however do not disclose the use of VEGF-deltaC156 or the chimeric heparin-binding VEGF-C polypeptide.

2.2 The purified cells as in claim 25 seem to be presently undistinguishable from the neural cells of the prior art and cannot be regarded as novel.

3. Inventive step:

The use of VEGF-C deltaC156 is not consider to involve an inventive activity since said compound was known from D3 as an alternative to native VEGF-C with a higher receptor selectivity. Since no particular surprising effect is associated with the use of said compound, claims 42 and 51 do not meet the requirements of the PCT in respect of inventive step (Article 33(2) and (3) PCT).
The combination of the VEGF-C or -D with any other neural growth factor is not considered as inventive since they represent mere alternative to the use of other neural growth factors as PDGFs already contemplated in D2.
The chimeric heparin-binding VEGF-C fusion polypeptide, although novel and having different properties as the native factor, is not seen as involving an inventive step either since said compound is not shown in the examples to bring a particular effect on neural cells and appear to be a mere additional derivative of VEGF-C.

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Re Item VIII:

Claim 1-4, 13-21,30,32 are not acceptable under Art. & PCT. The therapeutic application is functionally defined by a mechanism of action which does not allow any practical application in the form of a defined, real treatment of a pathological condition (disease).